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Original Article

Effect of total input fluid volume on the prognosis of patients with craniocerebral injury combined with hypernatremia

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Abstract: Hypernatremia is a common complication following craniocerebral injury and an independent predictor of mortality. To evaluate Association between total input fluid volume and the prognosis of patients with craniocerebral injury combined with hypernatremia. The study retrospectively collected 90 patients with craniocerebral injury combined with hypernatremia. The basic information, clinical data of the first day of hypernatremia occurred, and the average volumes of intravenous fluids, total fluid input and diuretic dosages following 3 days of hypernatremia occurred were gathered. Temperature, heart rate, Glasgow Coma Scale (GCS), chlorine, sodium, ventilation and the amount of Mannitol were correlation with the prognosis of this group of patients. After adjusted the other variables, GCS (B=-0.484, 95% CI=0.409-0.929), ventilation (B=3.489, 95% CI=-1.001-534.162) and total fluid volume (B=-0.001, 95% CI=0.998-1.000) became the independent risk factors of the prognosis. The incident of poor prognosis in the group with the amount of 2500~3200 ml within 24 hour is the least (3.1%), while the ones with ≤2500 ml and >3200 ml were 20.5% and 27.4%, respectively. In summary, there was an association between total input fluid volume and the prognosis, which the amount of 2500~3200 ml input fluid within 24 hour is beneficial for the prognosis of patients with craniocerebral injury combined with hypernatremia.

Keywords: Craniocerebral injury, hypernatremia, prognosis, total fluid input

Introduction

Hypernatremia is defined as a serum sodium concentration of over 145 mmol/L and reflects a disturbance of the regulation between water and sodium [1]. Hypernatremia is a common complication following craniocerebral injury with an incidence of 7~9% [2-4], and it can reach to 28.8% in the patients with craniocerebral injury of the neurosurgical intensive care unit (NICU) [5]. Hypernatremia is found to be an independent predictor of mortality in critically ill patients with a death rate of 41-66% [5, 6]. Waite et al. [7] found that hypernatremia was independently associated with a 40% increase in risk for hospital mortality and a 28% increase in intensive care unit (ICU) length of stay. Hypernatremia is a concomitant symptom in critically ill patients with craniocerebral injury and predicts the disease progression [8, 9].

There are various factors that can influence the death of patients with craniocerebral injury combined with hypernatremia, such as old age, mechanical ventilation use, low glasgow coma score (GCS) etc [10], and hypernatremia itself is a reason for death in this group of patients [5, 10]. But there is lack of researches to report association between input fluid volume and the prognosis of patients with craniocerebral injury combined with hypernatremia. This study was aim to explore the association between total input fluid volume and the prognosis of this group patients.

Materials and methods

Sampling

The present study employed a cross-sectional questionnaire survey by convenient sampling,

Table 1. Spearman's correlation between the demographic, clinical and therapeutic data and prognosis

	Variables	x (s)/n (%)	Spearman Values	*P* values
Demographic data	Sex (Male) [N(%)]	72 (54.1)	-0.035	0.688
	Age (Years)	56.04±14.4	-0.030	0.733
	Marital status [N (%)]		0.145	0.095
	Unmarried	7 (5.3)		
	Married	124 (93.2)		
	Widowed	2 (1.5)		
	Medical insurance (Yes) [N (%)]	45 (33.8)	0.032	0.715
Clinical data	Diagnosis [N (%)]		0.120	0.167
	Tumors	57 (42.9)		
	Brain trauma	46 (34.6)		
	Brain bleeding	30 (22.6)		
	Operation (yes) [N (%)]	111 (83.5)	0.087	0.321
	With other diseases (yes) [N (%)]	41 (30.8)	-0.042	0.634
	Diarrhea (yes) [N (%)]	3 (2.3)	0.056	0.556
	Temperature (°C)	38.0±0.9	0.345	<0.001**
	Heart rates (beats/min)	107.0±22.2	0.217	0.013*
	GCS (score)	9.2±4.0	-0.484	<0.001**
	Creatinine (μmol/L)	80.5±48.6	0.146	0.097
	Potassium (mmol/L)	3.7±0.6	-0.109	0.214
	Chloride (mmol/L)	113.3±9.0	0.336	<0.001**
	Sodium (mmol/L)	153.2±8.0	0.382	<0.001**
	Hemoglobin (g/L)	117.4±24.4	0.017	0.862
	NEUT (10^9/L)	11.7±24.4	0.149	0.129
	FPG (mmol/L)	10.0±4.5	0.081	0.560
	Volume of urine (mL/24 h)	3859.2±1183.4	0.024	0.920
Therapeutic data	Ventilation (yes) [N (%)]	12 (9.0)	0.374	<0.001**
	Hypotonic saline used (yes) [N (%)]	36 (27.1)	0.126	0.147
	Vasopressin used (yes) [N (%)]	9 (6.8)	-0.133	0.128
	Insulin used (yes) [N (%)]	53 (39.8)	0.141	0.106
	Xylitol used (yes) [N (%)]	39 (29.3)	0.099	0.257
	Mannitol used (mL/24 h)	386.9±331.6	0.205	0.018*
	Glycerol fructose (mL/24 h)	33.2±110.9	0.010	0.907
	Furosemide (mL/24 h)	7.5±19.5	0.082	0.350
	Fluid volume (i.v., mL/24 h)	2566.7±967.0	0.141	0.104

GCS: Glasgow Coma scale NEUT: Neutrophil count FPG: Fasting plasma glucose. *P<0.05; P<0.01.

with the entire participants was composed of 133 collecting anonymised computerized and handwritten clinical data and the medical records obtained from the first and second affiliated hospitals of Soochow University in China from Jan. 2013 to Jun. 2014. The inclusion and exclusion criteria were: 1) patients suffered from traumatic brain injury, brain tumor experienced operation, subarachnoid hemorrhage, brain hemorrhage; 2) blood sodium >145 mmol/L for at least three days; 3) without other severe conditions such as herniation, acute heart or lung or kidney failure; 4) without basic diseases; 5) age ≥18 years. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of the First Affiliated Hospital of Soochow University. Written informed consent was obtained from all participants.

Table 2. Multivariate Models: Predictors of the prognosis

Variables	B values	*P* values	95% CI
Temperature (°C)	0.657	0.195	0.714~5.216
Heart rate (beats/min)	0.019	0.480	0.966~1.076
GCS (score)	-0.484	0.021*	0.409~0.929
Chlorine (mmol/L)	0.078	0.444	0.885~1.321
Sodium (mmol/L)	0.110	0.310	0.903~1.380
Ventilation (yes vs. no)	3.489	0.014*	2.010~534.162
Mannitol (mL/24 h)	0.002	0.145	0.999~1.006
Total fluid volume (mL/24 h)	-0.001	0.028*	0.998~1.000

*P<0.05.

Table 3. The relation between the volumes of total input fluid and the prognosis

Volume (mL/24 h)	Prognosis [N (%)]		χ^2	*P*
	Good	Poor		
Total fluid				
≤2500	31 (79.5)	8 (20.5)	7.953	0.019*
2500~3200	31 (96.9)	1 (3.1)		
>3200	45 (72.6)	17 (27.4)		

*P<0.05.

Collection of data

We obtained information including (1) demographic data, (2) the clinical data at the day hypernatremia occurred (referred to clinical data), including diagnosis, operation, diarrhea, temperature, heart rate, other diseases, Glasgow Coma scale (GCS), fast glucose, blood sodium (taking the highest value if measured more than once), blood potassium, blood creatinine, hemoglobin, neutrophil count and volume of urine; (3) Therapeutic data including mechanical ventilation (yes or no); hypertonic saline, vasopressin, insulin and xylitol (used or not); the average volume of mannitol, glycerol fructose, furosemide and fluid volume from i.v. in 3 days after hypernatremia occurred. The fluid contained glucose saline, NS, hypotonic saline and nutrient solution.

The total fluid volume included the fluid volume from i.v. and digestive tract.

Outcomes

The prognosis of patients was divided into two categories of the good and the poor prognosis. The "good" included cured, improved, otherwise the poor which included unhealed, automatically discharged, died according to doctors' discharge records.

Statistical analysis

Statistical analysis was performed by SPSS for Windows version 18.0 (SPSS Inc., Chicago, IL). Descriptive data are presented as frequencies and percentages, mean and standard deviation. The correlation of binary variables was assessed using spearman correlation analysis. Furthermore, a multiple logistic regression was used to examine the adjusted association between the outcomes and covariates of interest. Chi-square tests were performed to determine the association between the volumes of total input fluid and the prognosis. *p* value less than 0.05 was regarded as statistically significant.

Results

Spearman's correlation between the demographic, clinical and therapeutic data and the prognosis

There were no obvious distribution changes in demographic data, clinical data and therapeutic data. In this group, 54.1% were male; average age was 56 years with minimum 22, maximum 83. 93.2% of them were married, 33.8% with medical insurance. 26 (19.5%) was poor prognosis which included 6 dead. Other clinical data and therapeutic data were shown in **Table 1**. Among these variables, temperature, heart rate, GCS, chlorine, sodium, ventilation and the amount of Mannitol were correlation with the prognosis of this group of patients (**Table 1**).

The predictors of the prognosis

After adjusted the other variables correlation with the prognosis shown in **Table 1**, GCS, mechanical ventilation and total fluid volume became the independent risk factors of the prognosis (**Table 2**).

The relation between the volumes of total input fluid and the prognosis

We further explored the reasonable amount of input fluid beneficial to this group of patients. As shown in **Table 3**, the incident of poor prognosis in the group with the amount of 2500~3200 ml within 24 hour is the least (3.1%), while the ones with ≤2500 ml and

>3200 ml were 20.5% and 27.4%, respectively.

Discussion

Hypernatremia often results in water to shift from intracellular fluid (ICF) to extracellular fluid (ECF), causing cell dehydration and shrinkage [11]. It is associated with increased risk of death and complications in some retrospective studies [12-14]. Hypernatremia and its related hyperosmolar state have the most common side-effect on neurologic function. The development of hyperosmolar can lead to brain cell shrinkag which can lead to permanent neurologic deficits [15]. Some researches have reported that severe hypernatremia can weaken the myocardial contractility, lead to rhabdomyolysis and renal failure even to death [15, 16]. So hypernatremia has been consistently associated with increased ICU mortality and length of stay [7, 17]. In our research, the death rate was 4.5% in the patients with craniocerebral injury combined with hypernatremia, which was lower than Darmon et al. finding that hospital mortality was 29.5% in patients with mild hypernatremia and 46.2% in those with moderate to severe hypernatremia [18]. The one possible reason was that there were 11.1% patients of automatic discharge, whose outcomes we did not know; the other reason might be that some patients in this study came from general units, while patients in the studies mentioned above were from NICU and critical ill.

In this study, we delightedly found that the amount of fluid intake were associated with prognosis in patients with craniocerebral injury combined with hypernatremia. By a reasonable excess gain of free water orally and as IV GS were clinical therapeutic strategy [19], considering these group of patients with the factors such as fever, ventilation. But excess water affects primarily the ECF and involves relatively equal gains of water and sodium leading to an ECF volume excess, which aggravates brain cells injury. We further found that the range of 2500-3200 ml was reasonable dose for these patients.

The other risk factors increasing the mortality of patients (poor prognosis) with craniocerebral injury combined with hypernatremia contained old age, lower GCS, mechanical ventilation, hypernatremia and cerebrovascular diseases themselves [10]. This study confirmed that lower GCS, mechanical ventilation were the independent risk factors of poor prognosis in these patients. Lower GCS revealed severe state of illness to some extent, which was associated with prognosis; on the other hand, patients with lower GCS were all in a state of unconsciousness who were loss of thirst sensation, while thirst sensation is the main protection mechanism against hypernatremia [15, 20]. Using mechanical ventilation was another risk factor predicting poor prognosis, because too much water can be carried out through the ventilator tube [10].

Other factors in this study were temperature, heart rate, serum sodium, serum chlorine, and mannitol usage, which were all positive correlated with prognosis. Fever can promote the evaporation of water via skin and respiratory tract, and profuse perspiration in the defervescence period can carry off plenty of water [21]. Mannitol can decrease the concentration function of kidney and drain hypotonic urine with less Na^+, so make overabundance of Na^+ accumulate in the body and promote hypernatremia occurred [22]. Increased heart rate is associated with decreasion of cardiac function and it is an independent risk factor of myocardial ischemia [23], so faster heart rate was related with the prognosis. The increase secretion of Cl^- and reabsorption of $HCO3^-$ by nephric tubule make nephric tubule secrete more Cl^- and reabsorb more Na^+, and then elevated serum sodium and influence the prognosis [7].

Limitation

Water volume orally might be not accurate because this study was a retrospective cross-sectional study. We enrolled the patients with the brain tumor experienced operation and brain hemorrhage, not single brain injury. Meanwhile, the sample of this study was small. A more elaborate and larger sample study and prospective study should be done in the future.

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Disclosure of conflict of interest

None.

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